LETTERS TO THE EDITOR

Regarding "Randomized comparison of percutaneous Viabahn stent grafts vs prosthetic femoral-popliteal bypass in the treatment of superficial femoral arterial occlusive disease"

Until recently, very few randomized studies have been performed on nonpharmacologic treatment of vascular patients. Therefore, the study by Kedora et al (J Vasc Surg 2007;45:10-16) comparing two interventional methods is more than welcome. The authors are to be congratulated for at least two reasons. One is that they performed a randomized study of this type, which is difficult, and the other illustrates the huge gap in study outline compared with randomized study on pharmacologic therapy. It is also welcome because it points to the need for properly designed studies on nonpharmacologic treatment. I have a few questions and comments for the authors:

1. The population of above knee reconstructions points to a rather benign problem of below groin disease, and there is no definition of lifestyle-altering claudication. Is it ethical to use a synthetic material in this situation?
2. Randomization was made by limb, but the limbs are not independent in one patient. Although not many bilateral reconstructions were done, this principle could skew the results.
3. No information is given on sample size calculation.
4. No information is given on whether the study was designed as a superiority or noninferiority trial, which also would influence the sample size.
5. The choice of bypass material was left to the discretion of the surgeon (polytetrafluoroethylene [PTFE] or polyester). Would it not have been more optimal to use the same material as in the stent graft (PTFE)?
6. The use of postoperative antiplatelet therapy was not standardized, meaning that 52% of the patients in the bypass group were given clopidogrel vs 90% in the stent graft group. This could be an advantage for the stent graft group.
7. There is no definition of 50% stenosis. How was that measured?
8. We have no information if outcome assessment was made in a blinded manner.

I believe that answers to the above questions would help readers in how to interpret the results of the study.

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Reply

The comments by Dr Bergqvist are welcome and offer additional insight to our study. The study was designed to evaluate all patients with superficial femoral arterial occlusive disease that were to be considered for revascularization. All patients with lifestyle-limiting claudication had failed attempts at conservative treatment alone. Although the study cohort included patients with claudication, as Dr Bergqvist states, it also included those patients with rest pain and tissue loss. These patient-specific data are outlined by Rutherford's clinical classification for ischemia in tabular form in the article.

We certainly do not argue that venous conduit is still considered the gold standard for vascular reconstruction in the lower extremities. Our study, however, was not designed to compare autologous conduit with synthetic material but, rather, to compare a percutaneous treatment option with open surgical revascularization using synthetic material in both treatment arms. Synthetic material has been studied and used in the reconstruction of superficial femoral arterial disease for a number of years by many surgeons as evidenced by numerous publications, including a more recent meta-analysis of >4000 limbs by Dorrucci[1] and in a second report by Bates et al.[2] The ethical consideration for any procedure must be assessed by each physician based on his or her own skill level and comfort level with the procedure to be considered. Each patient's symptoms must also be assessed individually before deciding to proceed with any intervention, and these two treatment options are certainly no different.

Randomization by limb was performed in all cases, and both limbs were randomized in 14 patients. There was no statistical difference in the patient demographic information, as is outlined in our paper. Because there are no differences in the demographic stratification and the limbs were prospectively randomized, the results should not be skewed by the subset of patients with bilateral randomization.

The study was intended as a noninferiority design, and 50 limbs in each group (100 limbs total) result in a margin of 24% if we use $\alpha = 0.05$ and power = 80%. The expanded polytetrafluoroethylene (ePTFE)–covered stent graft is considered noninferior to femoropopliteal surgical bypass if the true patency rate remains ≤24% of open surgical bypass. This outcome is, in fact, supported in our study's primary patency rate of 73% at 1 year for ePTFE covered stent grafts and 79% at 1 year for surgical femoropopliteal bypass.

The sample size was calculated before enrollment, allowing for adequate patient numbers to result in a study powered for a noninferiority trial. We felt that if we could demonstrate the outcome between the two treatment arms was equivalent, the advantage would be gained/realized in the percutaneous arm by a faster recovery and return to active life with a shorter hospital stay and less periprocedural pain.

Dacron and ePTFE grafts were allowed for use as a synthetic conduit at the discretion of the operating surgeon. The goal was to compare synthetic conduit of the most common types being used in current everyday practice with the ePTFE-covered stent graft. We felt that limiting the choice would have only diminished the value of the study. To our knowledge, no large study has demonstrated a clear statistically significant difference in the use of ePTFE vs Dacron for arterial bypass conduit above the knee.

Postoperative clopidogrel was used in 37 (93%) of the 40 patients in the stent graft group. Two patients refused the medication but did take aspirin, and one patient claimed an allergy to clopidogrel. In the surgical arm, 24 (52%) of 46 patients were treated with clopidogrel. Five patients were taking warfarin preoperatively, and they were continued on this postoperatively. Seventeen patients were treated with aspirin only at the recommendation of the treating physician. Although this discrepancy could be seen as an advantage for the stent graft group, there was no statistical difference between the surgical patients treated with clopidogrel and those that were not. In addition, our surgical arm patency data is comparable with historical studies; therefore, we believe there is no indication of any advantage for either group.[1-5] Additional studies specifically designed to evaluate any advantage the use of clopidogrel might offer in these two study arms would be helpful and are being considered at our own institution.

Follow-up was performed by each individual treating physician; therefore, outcome assessment was not blinded. Follow-up

arterial duplex was performed on all patients. Failure was defined as the presence of ≥50% stenosis within or immediately adjacent to the surgical bypass or ePTFE-covered stent graft. A stenosis of ≥50% was defined by B-mode imaging and color flow duplex scanning that demonstrated arterial velocities of ≥150 cm/s or a flow ratio of ≥2.5.

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Regarding: "Neovascularization: An 'innocent bystander' in recurrent varicose veins"

In this article, the authors present the preoperative duplex scanning (DS) and operative findings of a series of 500 consecutive patients treated by redo surgery between 1995 and 2005 for recurrent varices after surgery (REVAS) in the great saphenous vein (GSV) system.[1] All patients had previous surgery to the saphenofemoral junction (SFJ) but the initial surgery was performed over a wide time period in many institutions, presumably by a variety of surgeons.

DS identified a completely intact GSV system in 17.4%; incompetent thigh saphenous veins in 44.2% and GSV stump incompetence with one or more intact tributaries in 37.6%. Both a residual thigh GSV and an incompetent stump with intact tributaries were present in 16%. These facts testify to inadequate groin surgery.

Neovascularization was identified on DS in only 8.2% of limbs (41/500). However, in 27/41 of these, surgical exploration revealed a residual GSV stump with one or more tributaries. Each of the remaining 14 limbs had a residual incompetent thigh GSV.

The authors concluded that despite reports to the contrary, neovascularization occurs in a relatively small proportion of patients with REVAS.

Reflux from pelvic and abdominal veins as a cause of recurrent varicose veins is not mentioned in this report. This is a significant omission. It was present in 16.6% of cases in a worldwide survey of recurrent varicose veins.[2]

Since the initial description by Glass,[3] the prevalence of neovascularization as a cause of recurrent varicose veins has been debated. More than 50 articles both pro and con on the role of neovascularization have been published, but it is generally agreed that neovascularization occurs in 20% to 60% of cases following saphenous vein surgery.

So, the question arises: Why was the rate of neovascularization so low in this report?

As has been demonstrated in many studies, neovascularization develops principally when the high ligation (HL) is done flush with the femoral vein. The rate of technically inadequate flush HL in the initial surgery is very high in this report. The rate of incorrect, non-flush ligation in 71.0% of cases is not only surprising, but is unacceptable. This is probably related to the fact that patients were operated long ago when preoperative and postoperative DS were not done systematically. However, it may also be due to the fact that less than optimally trained surgeons under less than adequate supervision did the surgery. Immediate, postoperative US would have revealed the inadequate surgery earlier than the present time. Whatever the reason, the very high incidence of inadequate surgery explains the low rate of neovascularization.

Neovascularization is not an innocent bystander; it is a marker for properly performed surgery in the groin for venous insufficiency and may be associated with recurrent varicose veins. Fischer's series in which one surgeon did all of the operations and did them meticulously proves that fact.[4] This 34-year clinical follow-up study done by independent observers showed a 60% incidence of junctional and circumjunctional reconnections (neovascularization) after ligation of the true saphenofemoral junction and its related tributaries. Color-coded duplex ultrasonography documented the fact that the junction ligation had been performed correctly as shown by the absence of any patent proximal saphenous remnant. The neovascularization reflux originated at the site of the ligated saphenofemoral junction in 71% of limbs and from a nearby circumjunctional vein in the other 29%. Of the real junctional recurrences, 22 appeared as a tangled cluster, and 31 involved a single-lumen varix.

In Fischer's series, 27 recurrences in the 125 limbs studied were sufficiently symptomatic to warrant consideration of additional treatment. This incidence in a follow-up of 34 years with 60% neovascularization proves that the neovascularization is not just an innocent bystander. Its virtual absence in the present series is testimony to inadequate initial surgery.

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Reply

We would like to thank Dr Bergan for his attention to our report on a topic for which he has had an interest for a long time. He summarizes our key findings but failed to notice that we did report specific cross-groin/pelvic/vulval veins in seven limbs, in four of which they were the only source of reflux. This number is less than the 16% reported in the smaller multinational series of 199 limbs reported by Perrin.[1] However, among the 188 limbs with a GSV stump with one or more intact tributaries in our series, many of these tributaries drained from the pelvis, the vulva, or the abdominal wall. We believe it can be difficult to reliably determine the source of all tributaries to the GSV stump and, therefore, did not attempt to subcategorize this group further.